ORAL CONTRIBUTIONS

871 Atrial Tachycardia and Fibrillation. Anatomic, Cellular, and Molecular Considerations

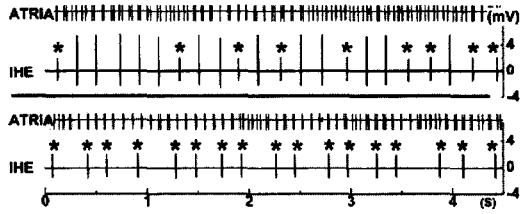
Tuesday, March 19, 2002, 4:00 p.m.-5:00 p.m.
Georgia World Congress Center, Room 160W

4:00 p.m.

871-1 A Novel Index Reveals Dual Pathway Conduction During Atrial Fibrillation

Youhua Zhang, Kent A. Mowrey, Saroja Bharati, Todor N. Mazgalev, *The Cleveland Clinic Foundation, Cleveland, Ohio, The Heart Institute for Children, Hope Children's Hospital, Oak Lawn, Illinois.*

Background: The function of atrioventricular nodal (AVN) dual pathway electrophysiology during atrial fibrillation (AF) remains unclear. We have validated (*Circulation* 2001;104:832-838) that His electrogram alternans can be used to determine which wavefront, the slow or the fast, reaches the His bundle. Specifically, the fast pathway (FPW) results in a small amplitude inferior His electrogram (IHE), while the slow pathway (SPW) produces large IHE. We hypothesized that this novel index can be applied during AF.
Methods: In 8 rabbit hearts, IHEs were recorded during AF in control and after a multistep surgical cut of posterior approach with subsequent morphological study.
Results: In 5 of the 8 hearts both high and low (top panel, *) IHE were present, indicating SPW and FPW, respectively. The FPW was responsible for 47± 24% of the conducted beats. In the remaining 3 hearts only SPW was operative during AF. Posterior approach modification damaged only the extension of the compact node. Importantly, this revealed an exclusive FPW conduction in all 8 hearts (bottom panel, low IHE), and was associated with an increase of the average His-His interval (200±13ms vs 267±36ms, p<0.001).
Conclusion: We have demonstrated for the first time that HE alternans permit visualization of dual pathway electrophysiology during AF. While both wavefronts are important players, the FPW becomes dominant after SPW modification. This novel index may be a useful guide during clinical ablations for control of ventricular rate during AF.



4:15 p.m.

871-2 Characterization of Focal Atrial Tachycardia Originating From Pulmonary Veins in Isolated Canine Left Atrium Using Optical Mapping

Rita Coram, Jianyi Wu, Tamana Takahashi, John Miller, Douglas P. Zipes, Jeffrey Olgin, *Indiana University School Of Medicine, Indianapolis, Indiana.*

Background: The precise location and cellular mechanism underlying focal atrial tachycardia originating from the pulmonary veins (PVs) have not yet been completely understood.
Methods and Results: Using optical mapping (256 mapping channels in 19 x 19 mm) in isolated canine left atrial preparations, we characterized the electrophysiological properties of focal PV activity induced by Isoproterenol. Based on the anatomic landmarks, definition of the primary PV ostium was to be between the left atrial chamber and the main PV trunk, the secondary ostium to be between the main PV and its branches, while the most distal atrial-PV junction to be between the pink atrial muscular sleeve and the white PV tissue. Under control conditions, in all 5 preparations, neither a PV potential nor spontaneous activity was observed. After exposure to 1uM of Isoproterenol for >15 min, sustained atrial tachycardia at a cycle length of 447.2±12.8 ms was induced in 2 preparations. Endocardial optical mapping showed the tachycardia to originate from a focal activity located at the primary PV ostium. A sharp, fractionated electrogram was also recorded with extracellular bipolar recording from the same location as the earliest activation determined by optical mapping (23.2±1.6 ms earlier than the other left atrial activation). These types of electrograms were not observed elsewhere in the PV during tachycardia. Overdrive pacing at a cycle length of 200 ms increased the tachycardia cycle length from 476.0±2.5 ms to 546.0±12.7 ms (p<0.05), which was consistent with focal automaticity rather than trigger activity. Local ablation (with 40 W for 60 sec) of the PV focus successfully eliminated atrial tachycardia in both preparations. There was no any spontaneous activity after ablation.
Conclusion: Spontaneous atrial tachycardia induced by Isoproterenol in isolated canine left atria originated from the primary PV ostium. The mechanism underlying this atrial tachycardia was a focal automatic activity rather than a triggered activity or a reentry.

4:30 p.m.

871-3 Apoptosis in Atrial Myocytes and Bcl2-Upregulation in Ventricular Myocytes Are Transient Phenomenona in Persistent Atrial Fibrillation

Richard Ammer, David Keane, Tom Aretz, Jeremy N. Ruskin, *Massachusetts General Hospital, Boston, Massachusetts.*

Background: The cellular changes from electrical to structural remodeling in persistent atrial fibrillation (AF) are not all known.
Methods: Myocardial samples from both atria and ventricles were obtained from the hearts of 43 goats which had undergone cardiac pacemaker (400bpm) implantation to induce AF in 29 goats. Goats were grouped according to AF duration, ranging from 2 to 430 days. Cardiac samples from the other 14 goats remaining in sinus rhythm were used as controls. Apoptosis was evaluated histo-and biochemically.
Results: Persistent AF for 3 months was characterized morphologically by an up to 9-fold increase in atrial myocyte apoptosis (TUNEL staining, 0.27 ± 0.05% vs. 0.03% ± 0.01%, p<0.001) and biochemically by agarose gel electrophoresis and Western blots for Bax, Bcl2, Cytochrome C, activated Caspase-3(p20); the percentage of ventricular myocytes labeled with Bcl2 was 5-times higher for goats in AF than in sinus rhythm (p<0.005). The percentage of apoptotic atrial myocytes, but not fibrocytes, correlated with the duration of AF (p<0.05). After peaks of apoptotic myocytes, atrial volume corrected by heart weight increased and fibrosis and glycogen deposition progressed over time (p<0.01). Goats in AF for 430 days revealed apoptosis in atrial and Bcl2 expression in ventricular myocytes at baseline levels (ns.)
Conclusions: In this model, programmed death of myocytes increases within 90 to 120 days of AF, despite enhanced Bcl2 expression and prior to atrial stretch and fibrosis, and reaches baseline levels after 210 to 430 days of AF. This transient phenomenon may contribute to the progression of electrical and structural remodeling associated with AF.

4:45 p.m.

871-4 Increased Open Probability of Single Cardiac L-Type Calcium Channels of Patients With Chronic Atrial Fibrillation: Role of Phosphatase 2A

Gunnar G. Klein, Frank Schröder, David Vogler, Arnd Schaefer, Axel Haverich, Bernhard Schieffer, Jürgen Tebbenjohanns, Helmut Drexler, *Hannover Medical School, Hannover, Germany.*

Background: The L-type calcium channel (LCC) plays a crucial role in the electrical remodeling of atrial fibrillation (AF). AF is associated with reduction of L-type calcium current density, due to a transcriptional downregulation of LCC. However, it is unclear, whether this current reduction is related solely to a decrease in channel number or to alterations in channel function. Hence, we performed a single LCC analysis to assess channel gating in human AF.
Methods: We used the cell-attached patch-clamp technique in isolated atrial human cardiomyocytes of 25 patients with sinus rhythm (SR) and 15 patients with chronic AF.
Results: On single channel level, peak average current was 1.7fold higher in AF than in SR, due to a 3.1fold higher open probability of LCC (table, * p<0.05). Since phosphatase 2A (PP2A) is known to selectively reduce LCC open probability via channel dephosphorylation, we hypothesized that PP2A expression or activity is reduced in AF. Okadaic acid, an inhibitor of phosphatases, increased channel open probability in SR, but not in AF, while western blot analysis of atrial homogenates of the same patient population revealed unchanged expression of PP2A.
Conclusions: This study shows for the first time, that single LCC activity is increased in AF, due to an increase in channel open probability. Our assessment of single channel data indicates impaired influence of PP2A on LCC, due to either general intracellular reduction of PP2A activity or impaired local interaction between PP2A and LCC in AF.

	Sinus Rhythm	Atrial Fibrillation
Peak Current (fA)	16.35 ± 2.34	27.25 ± 4.55*
Availability (%)	36.85 ± 2.96	31.75 ± 3.65
Open Probability (%)	3.93 ± 0.44	12.30 ± 1.53*

ORAL CONTRIBUTIONS

878 Mechanisms of Biventricular Pacing for Treatment of Congestive Heart Failure

Tuesday, March 19, 2002, 4:00 p.m.-5:00 p.m.
Georgia World Congress Center, Room 364W

4:00 p.m.

878-1 Comparative Effects of Ventricular Resynchronization Therapy in Patients With LV Systolic Dysfunction of Idiopathic or Ischemic Origin

Christophe Leclercq, Christine Alonso, Dominique Pavin, Gilles Rouault, Philippe Mabo, Jean C. Daubert, *University Hospital, Rennes, France.*

Biventricular pacing may improve symptoms and exercise tolerance in patients with chronic LV systolic dysfunction and intraventricular conduction delay. The aim of this study was to compare the long-term effects of Biventricular pacing in patients with dilated cardiomyopathy

(DCM) of ischemic origin and patients with idiopathic DCM. This study included 90 patients consecutively implanted with a Biventricular pacemaker between August 1994 and February 2000. Patients were retrospectively divided into two groups (idiopathic and ischemic) according to the results of a recent coronary angiogram. Symptoms and objective data were assessed before PM implant (pre-I) and 6 months (M-6) after, within the 2 groups. Results are summarized in this table :

Conclusion : Permanent Biventricular pacing provides significant and sustained improvement in symptoms, exercise tolerance and LVEF in both idiopathic and ischemic DCM patients.

	Total (n=90)			Idiopathic (n = 53)			Ischemic (n = 37)		
	Pre-I	M-6	P	Pre-I	M-6	P	Pre-I	M-6	P
QRS duration (ms)	185±26	158±19	<0.0001	184±25	159±18	<0.0001	186±2	158±21	< 0.0001
QRS axis (°)	-19±60	+53±76	<0.0001	-32±49	+55±75	<0.0001	-3±69	+50±78	0.002
NYHA class	3.3±0.5	2±0.6	<0.0001	3.3±0.5	2±0.5	<0.0001	3.4±0.5	2.1±0.6	<0.0001
Peak VO2 (ml.kg.min)	12±5	16±4	<0.0001	13±4	17±4	0.0003	10±4.7	15±4	0.02
LVEF (%)	21±6	26±8	0.0002	20±6	25±8	0.007	22±7	27±8	0.008

4:15 p.m.

878-2 Influence of Antitachy Pacing Location on the Efficacy of Ventricular Tachycardia Termination

Leon Krater, Barbara Lamp, Johannes Heintze, Bert Hansky, Juergen Vogt, Frank Warzok, Berthold Kramm, Reiner Koerfer, Dieter Horstkotte, *Heart Center North Rhine-Westphalia, Bad Oeynhausen, Germany, Bakken Research Center, Maastricht, Belgium.*

Background: Biventricular (BV) pacing is an important treatment option in patients (pts) with severe heart failure (HF). ICD-implantation with BV pacing is expected to help managing the risk of malignant tachyarrhythmias in this population.

Methods: The InSync ICD is a combined ICD and BV pacemaker with dual chamber detection and flexible ATP programming. The InSync ICD study enrolled 81 patients with severe HF (93% male, 64±9 y, CAD 56%, LVEF 25±7% LVEDD 71±11mm and NYHA 2.8±0.6). Inclusion criteria were NYHA II-IV, LVEF<35%, LVEDD>55mm and ICD indication. ICDs were randomly programmed to right-ventricular (RV)-ATP or BV-ATP. The VT termination efficacy and VT acceleration was evaluated for both pacing locations and for VT cycle length (CL).

Results: 457 spontaneous VT episodes occurred in 26 pts. 17 pts were programmed to RV-ATP, 9 patients to BV-ATP. Overall ATP efficacy was 84%, with 75% for RV-ATP and 91% for BV-ATP. Mean VT cycle length was significantly shorter for RV-ATP (369ms vs 389ms). After calculation for VTCL and initial therapy using logistic regression termination efficacy remained significantly (2.4 times) higher with BV-ATP.

Conclusion: BV-ATP in this limited population appears to be more effective in VT/FVT termination and may reduce the number of VT/FVT accelerations.

Spontaneous Episode ATP Therapy Efficacy (FVT=Fast VT Zone; VT=VT Zone)

ATP Site	Detection	#Episodes	terminated	accelerated
RV	FVT	50	31 (62%)	15 (30%)
	VT	154	123 (80%)	5(5%)
	VT/VFT	204	154 (75%)	23 (11%)
BV	FVT	57	43 (75%)	9 (16%)
	VT	170	163 (96%)	3 (2%)
	VT/FVT	227	206 (91%)	12 (5%)

4:30 p.m.

878-3 Reverse Mechanical Remodeling by Biventricular Pacing in Congestive Heart Failure: One-Year Results From Patients in Atrial Fibrillation in the MUSTIC (MUltisite STimulation In Cardiomyopathy) Study

Cecilia Linde, Christophe Leclercq, Serge Cazeau, Lukas Kappenberger, Richard Sutton, Christophe Bailleul, Jean-Claude Daubert, on behalf of the MUSTIC Study Group, *Karolinska Hospital, Stockholm, Sweden.*

Background: The MUSTIC study is a controlled multicenter trial, to assess the clinical efficacy of biventricular pacing (BIV) in patients with chronic NYHA III heart failure and intrinsic QRS >150 or RV paced QRS >200 ms. We recently reported symptomatic relief from the crossover phase (CO) with progressive improvements over a year. The aim of this study was to assess if left ventricular function improves over time in the group of patients with atrial fibrillation (AF) and slow ventricular rate either due to spontaneous rhythm or His-ablation.

Methods: Of 64 included patients 39 completed the 6 month CO single blind comparison of BIV and no-BIV excluding two patients who due to fast AF were not BIV paced. Of these 35 preferred and were programmed to BIV and followed longitudinally by clinical parameters, Doppler echocardiography and left ventricular (LV) ejection fraction measured by radionucleides.

Results: LV ejection fraction increased from 26.7 ± 6.8 % at randomisation (rand) to 30.4 ± 7.8 % after 1 year of BIV (p<0.05). LV function by Doppler echo i.e. diastolic filling time (DFT), left ventricular enddiastolic and systolic diameters (LVEDD, LVESD) and mitral regurgitation (MR) are given in the Figure.

Conclusion: In parallel with clinical benefits, left ventricular ejection fraction and mitral regurgitation improved by biventricular pacing in these patients with severe heart failure, atrial fibrillation and intraventricular conduction delay.

	Rand	BIV 9M	BIV 12M
	n = 67	n = 32	n = 29
LVEDD (mm)	70±9	68±10	68±8
LVESD (mm)	61±10	57±11	58±5
MR area (cm^2)	10.8±13.7	6.4±6.2	5.4±3.9*
DFT	346±99	357±133	405±143#

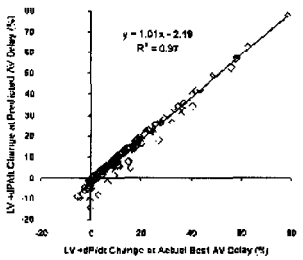
M=months, #p=0.06, *p<0.05, all compared to baseline

4:45 p.m.

878-4 Can the Optimum Dosage of Resynchronization Therapy be Derived From the Intracardiac Electrogram?

Angelo Auricchio, Andrew Kramer, Julio C. Spinelli, Jiang Ding, Yinghong Yu, Walter Hoersch, Christian Butter, Christoph Stellbrink, PATH CHF I & II investigator groups, *University Hospital, Magdeburg, Aachen, Berlin, Germany, Guidant CRM, St. Paul, Minnesota.*

We tested the hypothesis that the degree of pre-excitation required to provide optimum resynchronization can be predicted from the intrinsic atrioventricular (AV) interval. **Methods:** We tested 117 patients (NYHA class II-IV, EF < 30%) in the PATH CHF studies. 99 tests in 80 patients were used in the development data set (DST) and 50 tests/37 prospective patients constitute the test data set (TST). Intrinsic AV intervals were measured from the atrial event to the earliest peak in the ventricular leads. Linear regression coefficients between the AV delay that provided optimum dP/dt_{max} and the measured intrinsic AV interval were separately calculated for the cases with QRS>150 ms & QRS≤150 ms in the DST. Using these coefficients we calculated the estimated optimum AV delay for the cases in the TST and for all cases. The improvement in dP/dt_{max} at actual optimum AV delay (dP/dt_{opt}) was compared with the improvement in dP/dt_{max} obtained at the estimated optimum AV delay (dP/dt_{est}) both for the patients in the TST and for the entire population. **Results:** For the patients in the TST group dP/dt_{est}=.99*dP/dt_{opt}-1.75 (r^2=0.96, p<0.0001; ±0.03 p<0.0001, and ±0.43 p=0.0002 respectively). For the entire population, depicted in the Figure, dP/dt_{est}= 1.01*dP/dt_{opt}-2.19 (r^2=0.97, p<0.0001; ±0.01 and ±0.28 respectively, p<0.0001). **Conclusion:** The AV delay that provides optimum dP/dt_{max} can be reliably predicted from the intrinsic AV interval.



ORAL CONTRIBUTIONS

884 Noninvasive Testing: Predicting Future Events

Wednesday, March 20, 2002, 8:30 a.m.-10:00 a.m.
Georgia World Congress Center, Room 257W

8:30 a.m.

884-1 Value of Immediate Postoperative Electrocardiogram to Readjust Risk Stratification of Patients Undergoing Major Noncardiac Surgery

Stephane Rinfret, Carisi A. Polanczyk, Thomas H. Lee, *Brigham and Women's Hospital, Boston, Massachusetts, Centre Hospitalier de l'Universite de Montreal, Hopital Notre-Dame, Montreal, Quebec, Canada.*

Background: Despite preoperative stratification, additional information collected shortly after major non-cardiac (NC) surgery might help to reassess risk of major cardiac complications (MCC) and guide therapy. The usefulness of a simple electrocardiogram (ECG) performed in the recovery room is unknown.

Methods: Between 07/89 and 02/94, perioperative data and outcomes were collected on 4315 patients who underwent major NC procedures at Brigham and Women's Hospital. From this cohort, 3622 (83.9%) patients had an ECG performed in the recovery room.

Results: Univariate analysis showed a higher incidence of MCC (myocardial infarction, pulmonary edema, ventricular fibrillation or primary cardiac arrest, and complete heart block) in patients with signs of ischemia (ST depression or elevation, or T wave abnormalities) on the immediate postoperative (PO) ECG compared to those without ischemia (6.7 vs. 1.9%, p<0.001). Patients who presented signs of ischemia on PO ECG were older, more likely to be diabetic and treated with insulin, had a higher prevalence of coronary artery, peripheral, or cerebrovascular disease, hypertension, congestive heart fail-